

What is claimed:

- 1 1. A nucleic acid constructs for expression a small peptide, comprising:
2 a nucleic acid sequence encoding a signal peptide;
3 a nucleic acid sequence which encodes the pro-region of a somatostatin or a
4 functional fragment of analog thereof; and
5 a nucleic acid encoding a small peptide.
6
- 7 2. The construct of claim 1, wherein the nucleic acid sequence encoding the
8 signal peptide is from the pre-region of a somatostatin.
- 1 3. The construct of claim 1, wherein the small peptide is a small hormone.
- 1 4. The construct of claim 3, wherein the small peptide is an anti-diabetic peptide.
- 1 5. The construct of claim 4, wherein the anti-diabetic peptide is selected form the
2 group consisting of glucagon-like peptide-1 (GLP-1), exendin-4, gastric inhibitory
3 polypeptide and analogs thereof.
- 4 6. The construct of claim 1, wherein the construct further comprises a site
5 between the pro-region and the sequence encoding the small peptide.
- 6 7. The construct of claim 6, wherein the site between the pro-region and the
7 sequence encoding the small peptide can be cleaved.
- 1 8. The construct of claim 7, wherein the site is a multibasic, dibasic or
2 monobasic cleavage site.
- 1 9. The construct of claim 7, wherein the cleavage site is end protease cleavage
2 site.
- 1 10. The construct of claim 9, wherein the cleavage site is the cleavage site is
2 recognized by a pro-protein convertase.

1 11. The construct of claim 10, wherein the pro-protein convertase is furin,
2 subtilisin-related pro-protein convertase, PC1, PC2, PC6 or PC7.

1 12. The construct of claim 1, further comprising at least one regulatory sequence.

2 13. The construct of claim 1, wherein the small peptide is GLP-1.

1 14. A cell comprising:

2 an exogenous nucleic acid sequence which comprises a nucleic acid sequence
3 encoding a signal peptide and a nucleic acid sequence which encodes the pro-region of a
4 somatostatin or a functional fragment or analog thereof; and
5 a nucleic acid sequence encoding a small peptide;
6 the cell being capable of expressing the small peptide.

1 15. The cell of claim 14, wherein the nucleic acid sequence encoding the small
2 peptide is an endogenous genomic sequence.

1 16. The cell of claim 14, wherein the nucleic acid sequence encoding the small
2 peptides is an exogenous nucleic acid sequence.

3 17. The cell of claim 14, wherein the cell further comprises a site between the
4 pro-region and the sequence encoding the small peptide.

5 18. The cell of claim 17, wherein the site between the pro-region and the sequence
6 encoding the small peptide can be cleaved.

7 19. The cell of claim 18, wherein the cell is capable of expressing the small
8 peptide in mature form.

9 20. The cell of claim 18, wherein the cell is capable of expressing a fusion peptide
10 comprising the pro-region and the small peptide.

1 21. The cell of claim 14, wherein the cell is a primary cell.

2 22. The cell of claim 14, wherein the cell is a secondary cell.

1 23. The cell of claim 14, wherein the cell is a mammalian cell.

- 1 24. The cell of claim 23, wherein the cell is a human cell.
- 1 25. The cell of claim 23, wherein the cell is a fibroblast or a myoblast.
- 1 26. The cell of claim 14 is one in which somatostatin is not normally expressed.
- 1 27. The cell of claim 14, further comprising at least one regulatory sequence,
2 sufficient for expression of the exogenous nucleic acid sequence in the cell.
- 1 28. The cell of claim 14, wherein the sequence encoding the signal peptide is form
2 the pre-region of a somatostatin.
- 1 29. The cell of claim 14, wherein the small peptide is a small hormone.
- 1 30. The cell of claim 29, wherein the small peptide is an anti-diabetic peptide.
- 1 31. The cell of claim 30, wherein the anti-diabetic is selected from the group of
2 consisting of glucagon-like peptide-1 (GLP-1), exedin-4, gastric inhibitory polypeptide and
3 analogs thereof.
- 1 32. The cell of claim 18, wherein the site is a multibasic, dibasic or monobasic
2 cleavage site.
- 1 33. The cell of claim 32, wherein the cleavage site is an endoprotease cleavage
2 site.
- 1 34. The cell of claim 33, wherein the cleavage site is the cleavage site is
2 recognized by a pro-protein convertase.
- 1 35. The cell of claim 34, wherein the pro-protein convertase is furin, PACE4,
2 subtilisin-related pro-protein convertase, PC1, PC2, PC6 or PC7.
- 3 36. The cell of claim 18, wherein the cleavage site is a blood coagulation factor
4 cleavage site.
- 5 37. The cell of claim 14, wherein the small peptide is GLP-1.

38. A method of making a small peptide comprising culturing the cell of claim 14 to thereby obtain a small peptide.

39. The method of claim 38, wherein the small peptide is obtained in mature form.

40. The method of claim 38, wherein the small peptide is obtained as part of a fusion peptide which further comprises the pro-region of somatostatin or a functional fragment thereof.

41. A method of making a cell capable of expressing a small peptide, comprising: providing a cell; and, introducing into the cell a nucleic acid construct of any of claims 1, 6 or 7, to thereby obtain a cell capable of expressing a small peptide.

42. The method of claim 41, wherein the cell is a primary cell.

43. The method of claim 41, wherein the cell is a secondary cell.

44. The method of claim 41, wherein the cell is a mammalian cell.

45. The method of claim 41, wherein the sequence encoding the signal peptide is from the pre-region of a somatostatin.

46. The method of claim 41, wherein the small peptide is GLP-1.

47. A method of making a cell capable of expressing a small peptide, comprising: providing a cell; and, introducing into the genome of the cell an exogenous nucleic acid sequence which comprises the pro-region of a somatostatin linked to a nucleic acid sequence within the genome of the cell which encodes a small peptide to thereby obtain a cell capable of expressing a small peptide.

48. The method of claim 47, wherein the exogenous nucleic acid sequence further comprises a nucleic acid sequence encoding a signal peptide.

49. The method of claim 47, wherein the cell is a primary cell.

1 50. The method of claim 47, wherein the cell is a secondary cell.

1 51. The method of claim 48, wherein the sequence encoding the signal peptide is
2 from the pre-region of a somatostatin.

3 52. The methods of claim 47, wherein the small peptide is GLP-1.

1 53. A method of treating a subject, comprising:
2 administering to the subject an exogenous nucleic acid sequence comprising a nucleic
3 acid sequence encoding a signal peptide, a nucleic acid sequence which encodes the pro-
4 region of a somatostatin or a functional fragment thereof, and a nucleic acid sequence
5 encoding a small peptide, such that the small peptide is expressed.

1 54. The method of claim 53, wherein the sequence encoding the signal peptide is
2 from the pre-region of a somatostatin.

3 55. The method of claim 53, wherein the exogenous nucleic acid sequence further
4 comprises a site between the pro-region and the nucleic acid sequence encoding the small
5 peptide.

6 56. The method of claim 55, wherein the site between the pro-region and the
7 nucleic acid sequence encoding the small peptide can be cleaved.

8 57. The method of claim 53, wherein the small peptide is expressed in mature
9 form.

10 58. The method of claim 53, wherein the small peptide is expressed as part of a
11 fusion peptide further comprising the pro-region.

1 59. The method of claim 53, wherein the small peptide is a small hormone.

1 60. The method of claim 59, wherein the small peptide is an anti-diabetic peptide.

1 61. The method of claim 60, wherein the subject has diabetes.

1 62. The method of claim 60, wherein the anti-diabetic peptide is selected from
2 the group consisting of glucagon-like peptide-1 (GLP-1), exendin-4, gastric inhibitory
3 polypeptide and analogs thereof.

4 63. The method of claim 56, wherein the cleavage site is a multibasic, dibasic
5 or monobasic cleavage site.

6 64. The method of claim 56, wherein the cleavage site is an endoprotease
7 cleavage site.

8 65. The method of claim 64, wherein the cleavage site is the cleavage site is
9 recognized by pro-protein convertase.

1 66. The method of claim 65, wherein the pro-protein convertase is furin,
2 PACE4, subtilisin-related pro-protein convertase, PC1, PC2, PC6, or PC7.

3 67. The method of claim 56, wherein the cleavage site is a blood coagulation
4 factor cleavage site.

1 68. The method of claim 53, wherein the subject is a human.

1 69. The method of claim 53, wherein the disorder is characterized by
2 decreased expression of a small peptide.

1 70. The method of claim 53, wherein the small peptide is GLP-1.

2 71. A method of treating a subject, comprising:
3 administering to the subject the cell of any of claims 14, 19 or 20, to thereby
4 express the small peptide in the subject.

1 72. The method of claim 71, wherein the cell is obtained from the subject.

1 73. The method of claim 71, wherein the disorder is characterized by
2 decreased expression of a small peptide.

1 74. The method of claim 71, wherein the cell is a human cell.

- 1 75. The method of claim 71, wherein the cell is a primary cell.
- 1 76. The method of claim 71, wherein the cell is a secondary cell.
- 2 77. The method of claim 75, wherein the cell is a fibroblast or myoblast.
- 1 78. The method of claim 71, wherein the cell is autologous, allogeneic, or
2 xenogeneic.
- 1 79. The method of claim 71, wherein the small peptide is a small hormone.
- 1 80. The method of claim 79, wherein the small peptide is an anti-diabetic
2 peptide.
- 1 81. The method of claim 80, wherein the subject has diabetes.
- 1 82. The method of claim 80, wherein the anti-diabetic peptide is selected from
2 the group consisting of a glucagon-like peptide-1 (GLP-1), exedin-4, gastric inhibitory
3 polypeptide and analogs thereof.
- 4 83. A nucleic acid construct for expression of GLP-1, comprising:
5 a nucleic acid sequence encoding a signal peptide from the pre-region of
6 somatostatin;
7 a nucleic acid sequence which encodes the pro-region of a somatostatin or
8 a functional fragment or analog thereof; and
9 a nucleic acid sequence encoding GLP-1.